Renal injury in extreme obesity: the important role of aldosterone

Kidney International (2008) **74,** 1216; doi:10.1038/ki.2008.429

To the Editor: We read with interest the recent article by Serra *et al.*[1] detailing a variety of glomerular lesions (increased mesangial matrix, mesangial cell proliferation, podocyte hypertrophy, and glomerulomegaly) in extremely obese patients without clinical signs of renal dysfunction. Despite using a broad array of clinical and biochemical variables in their regression models, only body mass index was found to be a significant predictor of glomerular lesions in multivariate analysis.

We believe that serum aldosterone, if included in the analysis, would have likely emerged as another important predictor of obesity-related renal damage. Obesity is frequently associated with elevated levels of aldosterone.[2] In the obese state, oxidized fatty acids likely stimulate aldosteronogenesis;[3] *in vitro*, human adipocytes secrete potent mineralocorticoid-releasing factors.[4] Aldosterone is important in salt and water balance by acting on epithelial mineralocorticoid receptors, but its effects through mineralocorticoid receptors in nonepithelial tissues may be more important in the pathogenesis of chronic kidney disease. In animal models, unopposed aldosterone in the presence of high salt intake causes thrombotic and proliferative lesions in the glomeruli and renal vessels.[5–7] These pathologic lesions occur independent of blood pressure, reflecting a direct, nonepithelial, profibrotic effect of aldosterone on the kidney.

The increased glomerulosclerosis in these hyperaldosterone models typically result in severe proteinuria, a distinctly different phenotype from Serra *et al.*'s extremely obese subjects whose clinical renal function was normal. The authors, however, argue that the early lesions found in this study are potential harbingers of future, overt kidney disease. If so, then the glomerular lesions described in this study will likely progress to the more sclerotic lesions typified in the seminal animal studies discussed above.

The role of aldosterone in obesity-related kidney injury becomes more important as the discussion shifts toward potential treatment options. Serra *et al.* admit that their study does not address whether bariatric surgery could reverse the renal lesions seen on biopsy, and the authors cite a study in which angiotensin-converting enzyme inhibitors and statins ameliorate podocyte damage in obese rats.[8] In dogs fed a high-fat diet, the use of an aldosterone antagonist (compared to untreated controls) markedly attenuated obesity-induced glomerular hyperfiltration, sodium retention, and hypertension.[9] Because it will not be possible to offer all extremely obese patients bariatric surgery, it may be beneficial to check these patients' aldosterone levels and, if elevated, prescribe mineralocorticoid receptor blockers and salt restriction for renal protection. Alternatively, empiric treatment with mineralocorticoid receptor blockers and a low-salt diet may be undertaken even without aldosterone measurement, recognizing the possibility that mineralocorticoid receptor activation may also occur by elevated cortisol concentrations in obesity.[10]

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Response to 'renal injury in extreme obesity: the important role of aldosterone'

Kidney International (2008) **74,** 1216–1217; doi:10.1038/ki.2008.438

We appreciate the comments of Dr Bomback and Dr Klemmer on the possible relationship between aldosterone and obesity-related renal lesions.[1]

Obesity is associated with elevated levels of several hormones including aldosterone, leptin, adiponectin, cortisol, renin, and angiotensin.[2,3] Some of these hormones, such as leptin, have been associated with the production of renal lesions in animal models.[4]